## REMARKS

Claims 11, 17, and 54-64 are currently pending. No claims are amended. Claims 65-70 have been added. The new claims find support in the specification and do not add new matter. Specific support for the new claims is discussed in further detail below.

### Rejection of Claims 11, 17, and 54-64 Under 35 U.S.C. §112, Second paragraph

"Continuous lines"

The Office action states that claims 11, 17, and 54-64 are rejected under §112, second paragraph for alleged indefiniteness in the recitation of a "continuous line(s)."

Applicant respectfully disagrees and traverses the rejection.

The Office Action states that while the specification defines a line has having the dimensions of a line, the specification also teaches that the line could be made of a series of droplets that "'coalesce' into a 'circle'" (Office Action, page 4). Applicant notes that the wording identified in the Office Action be considered in context. Specifically, the language "series of droplets" that "coalesce" is present in paragraph 101, (page 26, starting line 1) which is reproduced below with the sentence of interest italicized:

> [0101] As used herein, the term "line" refers to a continuous distribution of an individual member of a repertoire having the physical shape of a line. A line as used herein may refer to a stream of an aqueous solution which is applied to a solid surface so as to form a line of solution. ***A line may alternatively refer to a series of droplets which are placed on a solid surface, and which coalesce to form a continuous line of solution.*** A line may alternatively refer to a solution or anhydrous compound which is deposited on a solid surface as a spray, provided that the solution or anhydrous compound is deposited in the form of a line. A

line may also refer to a tube with a lumen into which a member of a repertoire useful in the invention is placed. A line, useful in the present invention is preferably XX long and YY wide A line may also refer to a groove, or channel which is cut into a solid surface, such as by manually scratching the surface, or by automated means such as laser etching. As used herein, "cut" refers to producing a linear indentation in a solid surface by scratching, etching, depressing, deforming, chipping, or gouging the solid surface.

Applicant notes that the word “circle” is not present in the above paragraph.

Using the word search function, Applicant has identified three occurrences of the word “circle” in the specification (paragraphs 14, 113, and 151, corresponding to last paragraph starting on page 4, last paragraph staring on page 29, and last paragraph starting on page 38). As the use of circle is similar in each event, only paragraph 14 is reproduced below (emphasis added).

[0014] According to the invention, juxtaposition can be arrived at by, for example, creating a series of lines for each of the two repertoires, which intersect one another. The lines can be straight, substantially parallel lines, or curves, or combinations thereof; the only restriction is that all members of the first repertoire should be juxtaposed to all members of the second repertoire. ***Examples of complementary configurations include straight parallel lines, disposed at an angle to straight parallel lines; concentric circles or polygons, used together with a star of radial lines.*** The skilled person will be able to imagine many other systems being used to achieve a similar spatial configuration of the repertoire members according to the invention, all being characterised by the dispensation of some form of continuous line, stream, channel or flow corresponding to each member of the first repertoire, all of which has the ability to intersect all lines, streams, channels or flows corresponding to all members of the second repertoire. These include tubes for each member

> of the first repertoire which intersect tubes of the second repertoire, or channels cut in a solid material down which individual repertoire members can flow.

In each instance, circle is modified by the adjective "concentric". Moreover, the concentric circles are to be used together with a star of radial lines. Applicant submits that concentric circles can include, at most, one spot, at the center of the circles. Moreover, a filled in spot cannot be "used together with a star of radial lines" as described in the specification. Radial lines could not be present in a filled in circle as they would not be distinct.

Applicant respectfully requests that the Examiner identify language in context that suggests that a "continuous line" in the invention could be understood as a spot.

In the Office Action of May 3, 2007, it was noted that the use of "line" to include "spot" was repugnant to the definition. Applicant agrees.

Patent law does allow the inventor to be a lexicographer. However, if a term is to be understood as having a meaning contrary to the standard use, the meaning must be set for the clearly in the specification. This requirement is set forth in the MPEP 2173.05(a)(III) as follows (emphasis added):

> III. TERMS USED CONTRARY TO THEIR ORDINARY MEANING MUST BE CLEARLY REDEFINED IN THE WRITTEN DESCRIPTION
>
> Consistent with the well-established axiom in patent law that a patentee or applicant is free to be his or her own lexicographer, ***a patentee or applicant may use terms in a manner contrary to or inconsistent with one or more of their ordinary meanings if the written description clearly redefines the terms***. See, e.g., *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357, 52 USPQ2d 1029, 1033 (Fed. Cir. 1999) ("While we have held many times that a patentee can act as his own lexicographer to specifically define terms of a

> claim contrary to their ordinary meaning," ***in such a situation the written description must clearly redefine a claim term*** "so as to put a reasonable competitor or one reasonably skilled in the art on notice that the patentee intended to so redefine that claim term."); *Hormone Research Foundation Inc. v. Genentech Inc.*, 904 F.2d 1558, 15 USPQ2d 1039 (Fed. Cir. 1990). Accordingly, when there is more than one definition for a term, it is incumbent upon applicant to make clear which definition is being relied upon to claim the invention. Until the meaning of a term or phrase used in a claim is clear, a rejection under 35 U.S.C. 112, second paragraph is appropriate. In applying the prior art, the claims should be construed to encompass all definitions that are consistent with applicant's use of the term. See *Tex. Digital Sys., Inc. v. Telegenix, Inc.,* 308 F.3d 1193, 1202, 64 USPQ2d 1812, 1818 (Fed. Cir. 2002). It is appropriate to compare the meaning of terms given in technical dictionaries in order to ascertain the accepted meaning of a term in the art. *In re Barr*, 444 F.2d 588, 170 USPQ 330 (CCPA 1971).

Applicant has set forth a definition of line in the specification in paragraph 101 (page 26, starting line 1) as reproduced above. Having set off the term “line” in quotation marks after the phrase “as used herein,” one would understand that the definition provided is the intended definition. Applicant notes that continuous is also defined in the specification (paragraph 115, last paragraph starting on page 30). One reading the specification would not search for discontinuous phrases to provide a definition of line. Applicant further notes that the definition of line provided is consistent with standard definitions of the word “line.” From the *Riverside Webster’s II Dictionary*, copyright 1996, (copy enclosed), Applicant specifically notes definition 2 (reproduced below, emphasis added):

> 2. ***A thin, continuous mark,*** as that made by a pen applied to a surface.

Based on the statements of the prior Office Action, the definition clearly set forth in the specification, and the dictionary definition of “line,” Applicant submits that

one of skill in the art would understand the term line to be thin and continuous, and not a spot.

In paragraph 17 (last paragraph starting on page 5) of the specification, the advantage of using "lines" over "spots" is discussed. (emphasis added)

> [0017] The advantage of using intersecting lines, channels, streams or flows according to the present invention compared to compartmentalised combinatorial screening in the prior art is that as the size of the individual repertoires grow linearly, so does the number of dispensing steps required to screen all combinations of repertoire members. Thus, whereas screening techniques using wells would require 10,000 dispensing steps to screen a 100 by 100 repertoire, screening according to the present invention requires only 200 dispensing steps. Furthermore, since a single dispensing event is used to spatially array each member of each repertoire, comparison of interactions between individual members of the first repertoire with the members of the second repertoire with which it is juxtaposed will be more accurate. ***In addition, since the present invention uses intersecting lines rather than spots or intersecting channels rather than wells, less positional accuracy is necessary to ensure that all combinations of possible interactions are tested.*** Thus, if a two-dimensional screen is performed, and one line corresponding to a member of the first repertoire is offset by, for example, 1 mm, since it is arranged at an angle to all the lines from the second repertoire, it will still intersect all of them and therefore all combinations of interactions will still have been successfully tested. If, on the other hand, the spots corresponding to a member of the first repertoire are offset by, for example, 1 mm, they may miss the spots corresponding to the members of the second repertoire altogether and therefore many combinations of interactions will not have been tested. Therefore, the present invention is not only well suited to automated methods of

screening but also to manual methods, where positional accuracy cannot be guaranteed and the number of dispensing events must be limited.

Therefore, one reading the specification would understand that "spots" are not "lines."

Applicant submits that one reading the specification would clearly understand the meaning of the term "continuous line." Moreover, as the meaning of "continuous line" is consistent with what would commonly be understood to be the meaning of the term, no further definition in the claims is required.

If the Examiner maintains the rejection, Applicant respectfully request that the next Office Action cite at least complete sentences, if not complete paragraphs, to support the rejection.

Accordingly, Applicants request that the rejection be reconsidered and withdrawn.

**Rejection of Claim 11 Under 35 U.S.C. §102(b)**

The Office Action states that claim 11 is rejected under §102(b) as anticipated by Bussow et al. The Office Action states that Bussow et al. teach gridding cells onto filter membranes and "adding a 'stream'" of monoclonal antibody thus creating two- or three-chain polypeptides. A definition of the word "gridding" from the dictionary is provided to support the allegation that Bussow teaches gridding.

Applicant disagrees and traverses the rejection.

It is well settled law that to anticipate a claim, a prior art reference must teach, either expressly or inherently, each element of the claimed invention. *See, e.g., Perricone v. Medicis Pharmaceutical Corp.*, 432 F.3d 1368 (Fed. Cir. 2005).

Claim 11 requires a "first repertoire of single chain polypeptides deposited on the solid surface in a first series of continuous lines that do not intersect with each other, and said ***second repertoire*** of single chain polypeptides deposited on the solid surface in a second series of continuous lines." Bussow does not teach a second repertoire, arranged in continuous lines or otherwise. Bussow teaches contacting the filter ***homogeneously, and potentially sequentially, with single reagents*** to interact with polypeptides or polynucleotides on the membrane. In the legend of Figure 1, Bussow clearly teaches sequentially contacting the filter with reagents, not the checkerboard approach of the instantly claimed method. For example, Bussow states:

> Before antibody screening, filters were soaked with ethanol, and debris was wiped off with TBST-T… followed by washing… filters were blocked in blocking buffer… and incubated with antibody… after washing… filters were contacted with alkaline phosphatase-conjugated anti-mouse or anti-rabbit IgG….

Applicant submits that soaking, washing, blocking, and incubating steps as taught by Bussow would be understood to include contacting the entire filter sequentially and homogenously with reagents. Not depositing a second repertoire of single chain polypeptides as claimed. Moreover, the antibodies used by Bussow are not single chain polypeptides, as claimed, and the blocking agent is used to block sites on the filter not already bound to proteins, not to form interact with proteins already present on the membrane.

A repertoire is defined in the instant application as follows (emphasis added):

> [0099] The term "repertoire" as used according to the present invention refers to ***a group of members***, and also refers more narrowly to a group of members that share a common characteristic, such as a group of cells, a group of microorganisms, a group of proteins, a group of viruses, a group of nucleic acids, and a group of chemicals. More narrowly still, a "repertoire" may refer to ***variants*** of a particular type of member,

> that is, for example, a group of polynucleotide molecules, the group being based on a sequence which is mutated at specific positions to create variants of the basic sequence. Other examples of variants include, but are not limited to polypeptide sequence variants, cells which have been modified to express, for example, variant cell surface proteins which are derived from the same protein sequence, virus particles which have been modified to express variant envelope proteins which are derived from the same protein sequence, etc. Other members which may be used in a repertoire include cell type variants, nucleic acid sequence variants, virus strain variants, cellular fraction variants, small molecule variants, and the like. Generally, a repertoire includes more than 10 different variants. Large repertoires comprise the highest number of possible variants for selection and can be up to $10^{13}$ in size. Smaller repertoires are particularly useful, especially if they have been pre-selected to enrich for a particularly useful subset (for example, antibodies that bind cell surface markers, enzymes that catalyse a certain set of reactions, proteins that bind to other proteins etc) or to remove unwanted members (such as those including stop codons, incapable of correct folding or which are otherwise inactive). Such smaller repertories can comprise 10, $10^2$, $10^3$, $10^4$, $10^5$, $10^6$ or more polypeptides. Advantageously, smaller repertoires comprise between 10 and $10^4$ polypeptides.

For the sake of completeness, Applicant provides the following definition of group, again from the *Riverside Webster's II Dictionary*:

> A number of individuals or objects collected, situated, or classified together. –v. To place or be in a group.

It is noted that repertoire refers to ***members***, in the plural, and that the definition of group refers to ***individuals*** or ***objects***, again, in the plural. Applicant submits that one of skill in the art would understand that a repertoire refers to more than one member. Bussow does not teach "a second repertoire of single chain polypeptides

deposited on a solid surface" as recited in claim 11. Therefore the claim cannot be anticipated by Bussow.

The method of Bussow requires that if multiple probes are to be tested, multiple filters must be used. In the middle of the second column on page 5007, Bussow states:

> A set of three DNA filters (80 640 clones) were screened with cDNA probes.

The filters are shown in Figure 1 of Bussow. In part, the figure legend reads:

> Figure 1. Identification of cDNA clones expressing recombinant fusion proteins on high-density filters. (A) RGH-His antibody detection (gridding pattern of 3x3 surrounding ink guide dots as shown in lower right corner) (B) DNA hybridization with a GAPDH cDNA probe as described (3). (C) Screening with a polyclonal anti-GAPDH antibody.

The figure includes ***three separate parts*** that show ***three separate filters*** each tested for binding with a ***single probe***. Bussow does not teach a first repertoire of polypeptides and a second repertoire of polypeptides deposited on a solid surface as claimed in the instant application. The instantly claimed method allows for detection of interaction between members of a first repertoire of polypeptides with a second repertoire of polypeptides on a single solid support. This method is neither taught nor suggested by Bussow.

Moreover, Applicant submits that the definition of "grid" provided by with the Office Action in conjunction with the Bussow reference demonstrates that the "gridding" in Bussow is the use of "a network of uniformly spaced horizontal lines and perpendicular lines (***as for locating points on a map***)" (emphasis added). This common use of grid is also in the *Riverside Webster's II Dictionary* cited above which provides the following definition (emphasis added):

2. A pattern of lines forming squares, ***used as a reference for locating points*** on a map, chart, aerial photograph, etc.

Applicants submit that the "etc." includes bacterial colonies on a plate. Looking at the images in Bussow, one would clearly understand that "gridding" refers to the use of a grid as a reference for locating points, not as a series of lines. Applicant submits that as discussed herein, the term "continuous line" does not include spots. Bussow does not teach lines. Bussow only teaches spots.

The figure in Bussow clearly shows dots, not lines.

Applicant also provides herewith copies of pages from *Molecular Cloning: A Laboratory Manual*, Second Edition, copyright 1989. Step 2 of the method discusses gridding. Specifically, the reference states (emphasis added):

> 2. Using sterile toothpicks, transfer individual bacterial colonies onto the filter and then onto a master agar plate that contains the selective antibiotic but no filter. ***Make small streaks 2-3 mm in length (or dots) arranged in a grid pattern***. Each colony should be streaked in an identical position on both plates. Up to 100 colonies can be streaked onto a single 90-mm plate. Finally, streak a colony containing a non-recombinant plasmid (e.g., pBR322) onto both the filter and the master plate. This negative control is often useful an sometimes necessary to discriminate between specific annealing of the radioactive probe to a recombinant plasmid and non-specific background hybridization.

Applicant submits that the use of "grid" in the art and as shown in Bussow does not refer to lines, but instead to streaks or dots arranged in an organized, i.e., grid, pattern, not to a series of lines.

Accordingly, Bussow et al. does not teach each element of the instantly claimed invention and, therefore, does not anticipate. Applicants, therefore, request that the rejection be reconsidered and withdrawn.

Applicant has added new claims 66 and 67 which recite the limitation of "wherein the number of juxtapositions of members of the first repertoire and the second repertoire comprises 2 or 9 times the number of dispensing events." The amendment is supported, for example, in paragraph 209 and 205, respectively (first full paragraph on page 54, see also Figure 5a, and first full paragraph page 52). The number of interactions tested was 16 and the number of dispensing events was 8, in another manual matrix screen of 21 antigens against 16 scFvs, resulting in 336 interactions being tested using only 37 dispensing events (336/37 = 9.1). Applicant notes the open ended transitional phrase in the claim of "comprising" and that the number of juxtapositions can exceed two times the number of dispensing events.

In Bussow, each bacterial colony was generated by a distinct dispensing event (last paragraph, column 1, page 5007).

> Bacteria were grown in microtiter wells at 37 $^{o}$C overnight, and 9216 or 27 648 clones were gridded onto 222 mm x 222 mm filter membranes in a duplicate pattern (Fig. 1).

As Bussow does not teach interaction of bacterial proteins, the bacteria were gridded to provide distinct colonies, each colony requiring an independent dispensing event. For example, see Figure 1 of Bussow. To juxtapose the polypeptides, another dispensing event was required using the monoclonal antibody, which is not a single chain polypeptide as claimed. Therefore, the method of Bussow requires a higher number of dispensing events than the number of juxtapositions.

Newly added claims 66 and 67 cannot be anticipated by Bussow.

**Rejection of Claims 11, 17, 54-56, 59-61, and 64 Under 35 U.S.C. §102(b)**

The Office Action states that claims 11, 17, 54-56, 59-61, and 64 are rejected under §102(b) as allegedly anticipated by Rowe et al. The Office action states that Rowe et al. teach "methods for producing two-chain or three-chain polypeptides comprising utilizing an array immunosensor wherein vertical channels comprise

antibodies and adding samples flowed through horizontal channels…therein the vertical and horizontal channels are at 90$^{o}$ angles." The Office Action concludes that these teachings anticipate the claimed invention. Applicants respectfully disagree and traverse the rejection.

As noted above, in order to anticipate the claimed invention, a prior art reference must teach, either expressly or inherently, each element of the claimed invention. *See, e.g., Perricone v. Medicis Pharmaceutical Corp.*, 432 F.3d 1368 (Fed. Cir. 2005).

As with Bussow, Rowe does not teach "a second repertoire of single chain polypeptides deposited on the solid surface in a second series of continuous lines" as recited in both claim 11 and claim 17, the independent claims pending in the instant application.

Rowe teaches a method of screening biological samples, such as nasal swabs or serum, with monoclonal and polyclonal antibodies to detect the presence of clinical analytes in the biological sample.

First, the antibodies of Rowe are not single chain polypeptides as claimed (paragraph bridging pages 433 and 434). All of the antibodies taught by Rowe include at least two chains (Fab' fragments referred to in first full paragraph page 434). Therefore, the method of Rowe cannot anticipate the instantly claimed method that includes the use of single chain polypeptides.

Second, the method of Rowe includes the use of biological samples, not a repertoire of single chain polypeptides. Moreover, the antibodies of Rowe include antibodies specifically targeted to protein complexes, not single chain polypeptides, e.g., "purified D-dimer, high molecular weight D-dimer polymer (XL-FDP), and monoclonals DD-3B6/22 and DD-4D2/182 were a kind gift" (first paragraph page 434).

Third, the method of Rowe does not teach or suggest the claimed "method comprising the step of providing an array comprising a solid surface that includes said

first repertoire of single chain polypeptides deposited on the solid surface in a first series of continuous lines that do not intersect with each other, and ***said second repertoire of single chain polypeptides deposited on the solid surface in a second series of continuous lines*** that do not intersect with each other." As shown in the figures and clearly stated in the figure legend, Rowe teaches spots. The legend of Figure 1 states (emphasis added):

> (B) Application of sample. Samples are flowed through horizontally oriented channels in the sample flow chamber module. After rinsing, an appropriate detector molecule is flowed through the channels, and the substrate is again rinsed. If analyte is present in a sample, ***the corresponding spot fluoresces***.

Further, the abstract of Rowe states that the method is the use of:

> a patterned array of recognition elements immobilized on the surface of a planar waveguide… to "capture" analyte present in samples; bound analyte is then quantified by means of fluorescence. Upon excitation of the fluorescent label by a small diode laser, a CCD camera detects the pattern of fluorescent antigen:antibody complexes on the sensor surface. Image analysis software correlates the position of the fluorescent signals with the identity of the analyte. (quotes in original)

In the method of Rowe, a second series of continuous lines is neither taught nor desired. In Rowe, each of the first series of lines is separated by a blocking reagent to prevent non-specific binding. It is noted that the blocking agent is a single polypeptide, BSA, not a repertoire of polypeptides as required by the claims. In the paragraph headed with "Analysis of Samples." Rowe states (emphasis added):

> Following patterning of capture antibodies on the surface of the waveguide, another PDMS assay template was placed onto the patterned slide such that the six channels were horizontally oriented. Each channel

> was rinsed with 1 ml PBST and ***blocked for 10 minutes*** with a solution of PBST containing 1 mg/ml PBST. After rinsing, sample was introduced into each channel and incubated, with flow (0.3 ml/min), for 15 minutes.

It is well known that blocking agents are used to prevent binding to surfaces. The word "blocked" is well understood. No testing is required to understand the function of the step in the method of Rowe was designed to ***prevent the second protein from being deposited*** on the solid surface. Again, from *Molecular Cloning: A Laboratory Manual* (copy enclosed, emphasis added):

> Just as proteins transferred from the SDS-polyacrylamide gel can bind the nitrocellulose filter, so can proteins in the immunological reagents used for probing. The sensitivity of western blotting depends on reducing this background of non-specific binding by ***blocking potential binding sites with irrelevant proteins.***

In Rowe, the blocking is performed to ***prevent the formation of lines*** using the sample. As shown in Figure 2 of Rowe, when the analyte of interest is present, it is "captured" by the membrane in spots. The formation of a continuous line is neither taught nor desired as demonstrated by the use of the blocking agent to prevent the sample from binding except in locations where the fixed, multi-polypeptide antibody binds a cognate antigen in the sample. The method of Rowe is only operable when discrete spots can be identified.

The reference does not teach or suggest depositing two repertoires of single chain polypeptides in two series of continuous lines on a solid support as claimed in the instant application.

Accordingly, Rowe et al. does not teach each element of the claimed invention and Applicants, therefore, request that the rejection be reconsidered and withdrawn.

Newly added claims 65 and 69 recite the limitation of wherein ***each*** polypeptide of the first repertoire and each polypeptide of the second repertoire is deposited in a continuous line such that no member of the repertoire is not a continuous line. This limitation is supported, for example, in Figures 1 and 11 and in paragraph 113 (last paragraph starting on page 29). Rowe does not teach or suggest a second series of continuous lines. As noted above, Rowe uses a blocking reagent to ***prevent*** the formation of a second series of continuous lines. Therefore, Rowe does not teach or suggest each member of the repertoire deposited as a continuous line.

Newly added claims 66 and 70 recite the limitation of wherein the first repertoire of polypeptides and the second repertoire of polypeptides are arrayed ***prior to interaction of the polypeptides*** of the first repertoire with the polypeptides of the second repertoire. This limitation is supported, for example, in paragraph 18 (first full paragraph page 6). Applicant notes that arraying the polypeptides prior to interaction of the polypeptides does not require the use of two filters. In Rowe, the second polypeptide is "captured" by the first polypeptide. ***Therefore, the second polypeptide cannot be arrayed on the solid support in the absence of the first polypeptide***. The claims cannot be anticipated by Rowe.

**Rejection of Claims 11, 17, and 54-64 under 35 U.S.C. §103(a)**

The Office Action states that claims 11, 17 and 54-56, 59-61 and 64 are rejected under §103 as unpatentable over the teachings of Rowe et al. in view of Stevens et al. The Office Action applies Rowe et al. as described above, but notes that Rowe et al. does not teach making $V_H$-$V_H$ or $V_L$-$V_L$ two-chain polypeptides or two-chain polypeptides bound to antigen to generate a three-chain polypeptide. The Office Action states that Stevens et al. teaches methods of making recombinant antibody subunit dimers and screening against antigen, and concludes that it would have been obvious to modify the method of producing two- or three-chain polypeptides as allegedly taught by Rowe et al. to include the $V_H$-$V_H$ and $V_L$-$V_L$ dimers taught by Stevens et al. Applicants disagree and traverse the rejection.

It is well established that to render a claim obvious, the prior art reference (or references when combined) must teach or suggest all the claim limitations. *In re Royka*, 490 F.2d 981, 180 U.S.P.Q. 580 (C.C.P.A. 1974).

As stated above, Rowe et al. does not teach each element of the invention recited in independent claims 11 and 17 (nor does Rowe et al. teach each element of the invention recited in dependent claims 54-64 or newly added claims 65-70).

Stevens et al. essentially describes methods of making recombinant antibody dimers in which at least one codon of a nucleic acid sequence is modified (abstract) and hence is in a different field than Rowe et al (which describes an immunoassay using an immunosensor for detection purposes). Like Rowe, Stevens also does not mention or suggest making any polypeptide repertoires. Were the skilled person to read Stevens et al., although they may be been motivated to use the methods described therein to produce antibody dimmers, the skilled person would not, on reading Stevens alone or in combination with Rowe et al., have been motivated to abandon this teaching and instead make repertoires of molecules as described by the present application and then screen these against one another according to the claimed method. Thus, even if the teachings of Rowe et al. and Stevens et al. are considered together, the resulting combination does not teach the claimed method.

There is no teaching in Stevens et al. that supplements the deficiencies Rowe et al. to arrive at the claimed invention. Thus, even if the teachings of Rowe et al. and Stevens et al. are considered together, the resulting combination does not teach a method of generating a two- or three-chain polypeptide by depositing a first and second, and optionally third series of continuous lines on a surface such that the lines of each series intersect with the lines of the other series, such that each member of each repertoire is juxtaposed with each other member of each other repertoire. Accordingly, the combination cited in the Office Action does not teach each limitation of the amended claims, and does not render the instant claims *prima facie* obvious.

Applicants, therefore, request that the rejection be reconsidered and withdrawn.

**Rejection of Claims 11, 17, and 54-56, 59-61, and 64 under 35 U.S.C. §103(a)**

The Office Action states that claims 11, 17, 54-56, 59-61, and 64 are rejected under 35 U.S.C. §103(a) as being unpatentable over Skerra et al. (Anal. Biochem. 196:151-155, 1991), and Pardos et al. (US Patent No. 4,010,077).

Applicant disagrees and respectfully traverses.

The Office Action states that Skerra teaches a filter screening method comprising streaking a petri dish containing agar and a membrane with bacterial colonies expressing Fab fragments, but that Skerra does not teach streaking multiple continuous lines. The Office Action states that Pardos teaches a tool and method for streaking multiple lines. Further, the Office Action states that it would have been obvious to practice the method of Skerra using the device of Pardos to yield the instant invention.

Applicant respectfully disagrees and traverses the rejection.

Skerra fails to suggest the instantly claimed method for at least one of the same reasons as each Bussow and Rowe. Skerra fails to provide a second repertoire of polypeptides as required by the claimed invention. Skerra, as Bussow, provides a single polypeptide to be contacted with a repertoire of spots. Skerra teaches sequential and homogenous exposure of the solid support to a series of reagents (see, e.g., Detection of Antigen Binding section, starting bottom column 1, page 152). In part, the method recites:

> The capture membrane was incubated with biotinylated lysozyme (~ 1 µg/ml) in PBS/Tween for one hour. The membrane was washed three times in PBS/Tween and incubated for one hour with a covalent

> streptavidin/alkaline phosphatase conjugate at a dilution of 1:2000 in PBS/Tween (Amersham UK, RPN 1234). The membrane was washed…

In each step, the ***entire membrane*** is exposed to each of the reagents. This is clearly distinct from the claimed invention in which a second repertoire of single chain polypeptides are deposited on a solid surface in a second series of continuous lines. Even if one were motivated to use the device of Pardos to streak bacteria in lines in conjunction with the method of Skerra, which one would not, Skerra does not provide a second repertoire of polypeptides or a method to deposit them in continuous lines. The device of Pardos can only be used to deposit micro-organisms in lines on a solid surface. Skerra does not teach or suggest methods of detection of interaction of micro-organisms or polypeptides produced thereby.

Moreover, the device of Pardos is not designed for simultaneous streaking of multiple samples, but instead for use to sequentially streak samples using a single device. For example, the specification states (col 1, lines 19-38, 53-58, emphasis added):

> In a typical procedure the physician or technician will first streak the specimen in an initial direction along one side of the plate with the loop. He will then sterilize the loop over a Bunsen burner flame or the like, and ***continue streaking or spreading the specimen*** from the first streaked area across a second area. At that point he will again sterilize the loop and ***streak or spread the specimen*** from the second streaked area across a third area of the dish. Further streaking operations across the growth medium can be performed, with the streaking loop being sterilized between each separate streaking step. ***The purpose of the successive streaking steps is to progressively dilute the amount of bacteria on the loop or swab as it spreads the bacteria over each streaking area.*** This will sufficiently separate the individual bacteria in the specimen from one another, particularly in the last area streaked, so that visible colonies

> of growth result from each viable cell, with the colonies being spaced from one another to facilitate their study and identification….
>
> Accordingly, it is an object of the present invention to provide a new and improved bacteriological transfer loop which will permit ***streaking or plating of a specimen*** on a growth medium by the physician without need for successive sterilization steps between successive streaking operations.

Therefore, using the teachings of Pardos, one would not be motivated to deposit a repertoire of single chain polypeptides on a solid surface. The device of Pardos is designed to deposit a single micro-organism on a solid support. Applicant notes that Pardos teaches streaking of ***the*** specimen or ***a*** specimen, referring to a single specimen rather than a repertoire. It is noted that the steps shown in Figures 2-4 pointed to in the Office Action show the dilution method recited in column 1 reproduced above. It does not teach the deposit of a repertoire of single chain polypeptides.

The combination of Skerra and Pardos does not suggest the claimed method of the invention in which a first repertoire of polypeptides and a second repertoire of polypeptides are deposited on a solid support.

Withdrawal of the rejection is respectfully requested.

Moreover, none of the newly added claims are obvious over Skerra in view of Pardos.

The Office Action states that claims 11, 17, 54-56, 59, 61, and 64 are unpatentable over Rodenberg in view of Pardos.

Applicant disagrees and respectfully traverses.

The Office Action states that Rodenberg teaches a modified colony-life method comprising plating bacterial cells transformed with scFv/ phagemid constructs

onto agar plates, transferring the colonies to a membrane, coating the membrane with antigen (singularly and homogeneously), and adding another antibody to the membrane (again singularly and homogenously). The Office Action further states that Rodenberg does not teach the manner of plating which is allegedly provided by Pardos.

As discussed above, Pardos does not teach a method depositing a repertoire of polypeptides on a surface. Instead, Pardos teaches a device for diluting a single sample without having to sterilize the loop between steps. Therefore, Pardos cannot make up for the deficiencies in Rodenberg.

For the sake of completeness, Applicant submits that Rodenberg fails for not providing a second repertoire of single chain polypeptides deposited in continuous lines on a solid support as instantly claimed. Rodenberg only teached homogenous and sequential contact of the filter with various reagents (top of column 2, page 2). This is clearly distinct from the instant invention for the reasons discussed above in relation to Skerra which teaches a similar, sequential, homogeneous exposure of the solid support to a series of reagents.

Withdrawal of the rejection is respectfully requested.

**Obviousness-type Double Patenting**

The Office Action states that claims 11, 17, and 54-64 are provisionally rejected on the ground of non-statutory obviousness type double patenting as being unpatentable over claims 1-18 of co-pending patent application 10/161,145.

The Office Action states that claims 11, 17, and 54-64 are provisionally rejected on the ground of non-statutory obviousness type double patenting as being unpatentable over claims 1-23 of co-pending patent application 11/413,427.

The Office Action states that claims 11, 17, and 54-64 are provisionally rejected on the ground of non-statutory obviousness type double patenting as being unpatentable over claims 56-68 and 78-86 of co-pending patent application 09/888,313.

As the rejections are provisional double patenting rejections, Applicant requests that the rejections be held in abeyance until allowable matter is indicated in one of the cases.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

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Respectfully submitted,

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